

IN THE U.S. PATENT AND TRADEMARK OFFICE

Applicant: Yusuke NAKAMURA et al.

Conf.: 7091

Appl. No.: 10/060,301

Art Unit: 1637

Filed: February 1, 2002

Examiner: Y. J. Kim

For: A METHOD FOR SNP (SINGLE NUCLEOTIDE POLYMORPHISM)
TYPING

DECLARATION UNDER 37 C.F.R. § 1.132

Commissioner for Patents
PO Box 1450
Alexandria, VA 22313-1450

Sir:

I, Dr. Yusuke Nakamura, hereby declare as follows:

1. I am a Japanese citizen, receiving mail at 1-17-33, Azamino, Aoba-ku, Yokohama-shi,
Kanagawa 225-0011, Japan.

2. I am presently employed as ____ (position) _____ in the ____ (company or
institute) _____. A copy of my Curriculum Vitae is attached.

3. I am a co-inventor of the subject matter of the above-identified U.S. Patent application. I
am familiar with the specification and pending claims, and with the prosecution history of the
application.

4. The Examiner has rejected claims 1, 3, 5 and 7 of the application as being obvious in view of Mein et al., *Genome Research* 10:330-343 (2000) in view of Wang et al., *Science* 280:1077-1082 (1998). Furthermore, claims 2, 6 and 8 are rejected as being obvious over Mein et al. and Wang et al. in further view of Brooks et al., U.S. 2001/0046670.

5. The Examiner asserts that Mein et al. disclose multiplex amplification of polymorphic loci followed by detection of SNPs by an INVADER assay method. In the Mein reference, 36 SNP sites were typed by 10 ng of DNA. The Examiner admits that both the number of primer pairs and the amount of DNA used by Mein et al. are outside the scope of the present claims.

6. The Examiner asserts that Wang et al. disclose detection of SNPs by simultaneously amplifying up to 558 loci.

7. The Examiner asserts that Brooks et al. disclose "hot start" PCR.

8. The essence of the Examiner's reasoning is that Mein and Wang both describe multiplex amplification of DNA that includes SNPs, and that modification of the reaction in terms of alteration of the amount of reagents used, as in the presently claimed invention, is "mere optimization", thus obvious, unpatentable modification of the prior art. In this regard, I note that

Brooks et al. is cited only for its teaching of "hot start" PCR methods and adds nothing to the question of obviousness of the principal invention.

6. To demonstrate that the results of successful typing of at least 98% of loci by the instantly claimed method using an amount of DNA at the lower end of the range recited in the present claims, that is at a ratio of 0.1 ng of DNA per SNP site to be typed, 96 loci were simultaneously typed for 20 samples of genomic DNA using the method described in Examples 1 through 3 of the present application, except that 10 ng of DNA were used as the starting material for the amplification reaction, and only SNP loci 1 through 96 described in Example 2 were typed, so that a 96-well plate could be conveniently used.

7. The results of the experiment are shown in the attached Table I. "11" means the sample is homozygous for allele 1. "22" means the sample is homozygous for allele 2. "12" means the sample is heterozygous. "XX" denotes a failure of typing of the locus for that sample. The final column shows the percentage of loci successfully typed in the experiment.

8. The data show that, for all 20 of the samples typed, at least 98% of the loci were successfully typed, and in 14 of 20 samples 100% of the loci were successfully typed.

9. Based on the results of Wang et al., about 85% of the loci would be successfully typed at

the level of simultaneous analysis of 96 loci. See the top of the third column of page 1080 of the reference. Therefore, the finding that more than 98% of 96 loci were successfully typed simultaneously using the method of the present invention must be taken as unexpected.

10. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Date: _____

By _____
Dr. Yusuke Nakamura

TABLE I

	SNP1	SNP2	SNP3	SNP4	SNP5	SNP6	SNP7	SNP8	SNP9	SNP10	SNP11	SNP12	SNP13	SNP14	SNP15	SNP16	SNP17	SNP18	SNP19	SNP20	SNP21	SNP22	SNP23
001	22	22	11	22	22	11	22	11	11	11	22	22	22	11	22	22	22	11	22	12	22	22	22
002	11	12	12	22	22	12	22	11	11	11	22	22	22	11	22	22	22	12	12	12	22	22	22
003	12	12	11	22	22	11	22	12	12	12	12	12	12	11	22	22	12	11	22	22	22	22	22
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015	22	12	11	22	22	11	22	11	11	11	22	22	22	12	22	22	22	12	22	22	22	22	22
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SNP24	SNP25	SNP26	SNP27	SNP28	SNP29	SNP30	SNP31	SNP32	SNP33	SNP34	SNP35	SNP36	SNP37	SNP38	SNP39	SNP40	SNP41	SNP42	SNP43	SNP44	SNP45
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SNP46	SNP47	SNP48	SNP49	SNP50	SNP51	SNP52	SNP53	SNP54	SNP55	SNP56	SNP57	SNP58	SNP59	SNP60	SNP61	SNP62
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